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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/656,907	09/08/2003	Huiping Guan	PC23544B	9254

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AGOURON PHARMACEUTICALS, INC.
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EXAMINER

ANDERSON, REBECCA L

ART UNIT	PAPER NUMBER
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1626

DATE MAILED: 12/13/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/656,907	Applicant(s) GUAN ET AL.	
	Examiner Rebecca L. Anderson	Art Unit 1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 September 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 18-36 is/are pending in the application.
- 4a) Of the above claim(s) 23 and 25-28 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 18-22, 24 and 29-36 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>9/8/2003</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 18-36 are currently pending in the instant application. Claims 23 and 25-28 are withdrawn from consideration as being for non-elected subject matter and claims 18-22, 24 and 29-36 are rejected.

Election/Restrictions

Applicant's election with traverse of Group I in the reply filed on 20 September 2005 is acknowledged. The traversal is on the ground(s) that there is no undue burden to search all of the claims. This is not found persuasive because the inventions are independent and distinct because there is no patentable co-action between the groups and a reference anticipating one member will not render another obvious. Each group is directed to art recognized divergent subject matter, which require different searching strategies for each group. Moreover, the examiner must perform a commercial database search on the subject matter of each group in addition to a paper search, which is quite burdensome to the examiner.

The requirement to elect a specific compound, as found on pages 3-5 of the previous office action, is withdrawn.

Therefore, the elected invention for search and examination is the process for preparing products of the formula (I) as found in claims 18-22, 24 and 29-36.

The requirement is still deemed proper.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

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art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Newly added claims 20-22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Specifically, claim 20 claims wherein the compounds of the formulas (IV) and (V) are reacted in the presence of an organic solvent with a coupling agent. Dependent claims 21 and 22 specify the organic solvent is dimethylformamide or tetrahydrofuran (claim 21) and specify the coupling agent as dicyclohexylcarbodiimide, DEAD, EDC or HOBt. The subject matter claimed in claims 20-22 is considered new matter as the general synthetic procedure found on page 69, which provides support for the process as claimed in claims 18 and 19 discloses the reaction of the substituted 2-oxindole (formula IV) with the substituted 3-carboxy-5-formylpyrrole (formula V) as being in the presence of a base and a solvent, does not provide support for the reaction of the compounds of the formulas (IV) and (V) in the presences of an organic solvent and a coupling agent. Furthermore, the solvent exemplified for the reaction of the substituted 2-oxindole and the substituted 3-carboxy-5-formylpyrrole does not include the solvent tetrahydrofuran. There are no examples, nor is there any general description for the reaction of the substituted 2-oxindole (formula IV) with the substituted 3-carboxy-5-formylpyrrole (formula V) with a coupling agent, let alone with the specific coupling agents claimed in claim 22. There is also no example nor general description with any organic solvent or tetrahydrofuran. The only

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description found in the instant specification which includes the use of an organic solvent and a coupling agent is the process of reacting the compounds of the formula (II) and formula (III) to prepare the compounds of the formula (I) (page 71). The description found on page 71 only provides support for the use of an organic solvent and a coupling agent for the process of reacting the compounds of the formulas (II) and (III) and not for the process of reacting the compounds of the formulas (IV) and (V). This rejection can be overcome by deleting the new matter from the claims, or by canceling the claims.

Claims 18-22, 24 and 29-36 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of synthesizing a compound of formula (I) comprising reacting a compound of formula (II) with a compound of formula (III) in the presences of an organic solvent and a coupling agent does not reasonably provide enablement for a method of synthesizing a compound of formula (I) comprising reacting a compound of formula (II) with a compound of formula (III) without an organic solvent and a coupling agent. Also, while being enabling for forming a compound of formula (II) by reacting a compound of formula (IV) with a compound of formula (V) in the presence of a solvent and a base, the specification is not enabling for forming a compound of formula (II) by reacting a compound of formula (IV) with a compound of formula (V) without the presence of a solvent and a base as instantly claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make/use the invention commensurate in scope with these claims.

As stated in the MPEP 2164.01 (a), "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue."

In In re Wands, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have need described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

In the instant case, the nature of the invention of claims 18-22, 24 and 29-36 is the process for preparing compounds of the formula (I) comprising reacting a compound of formula (II) with a compound of formula (III) (claims 18-22, 24 and 29-36). Claims 19-22 claim wherein compound (II) is formed by reacting a compound of formula (IV) with a compound of formula (V) (claim 19), in the presence of an organic solvent with a coupling agent (claim 20) wherein the organic solvent is dimethylformamide or tetrahydrofuran (claim 21) and the coupling agent is dicyclohexylcarbodiimide, DEAD, EDC or HOBt (claim 22). Claims 24 and 29-36 claim the preparation of specific compounds of the formula (I), for example, 5-[5-fluoro-2-oxo-1,2-dihydro-indol-(3Z)-ylidenemethyl]-2,4-dimethyl-1H-pyrrole-3-carboxylic acid (2-hydroxy-3-morpholin-4-yl-propyl-amide.

The state of the prior art and the predictability or lack thereof in the art

The state of the prior art and the predictability or lack thereof in the art is that a method of synthesizing a compound of formula (I) by reacting the compounds of the formula (II) and (III) would require additional reaction conditions and reagents in order to condense the compounds of the formulas (II) and (III). For example, coupling agents are useful for enhancing bonding by promoting or establishing a stronger bond, while solvents are useful for dissolving the reactants. Furthermore each step of a synthesis involves a chemical reaction, and reagents and conditions for each of these reactions are designed to give a good yield and a pure product with as little work as possible.

The amount of direction or guidance present and the presence or absence of working examples

The only direction or guidance present in the instant specification is found on pages 69-71 wherein substituted 2-oxindoles, formula (IV), substituted 3-carboxy-5-formylpyrrole, formula (V), compounds are reacted in the presence of a solvent and a base for the preparation of the products of the formula (II), 5-(2-oxo-1,2-dihydroindol-(3Z)-ylidenemethyl)-1-H-pyrrole-3-carboxylic acid compounds. The products of the formula (I) are prepared by the reaction of the compounds of the formula (II) and formula (III), $ZCH(R_5)-CR_4(OH)-CHR_3NH_2$, in the presence of an organic solvent and a coupling agent. Examples of solvents and bases are found on page 70 and examples of organic solvents and coupling agents are found on page 71. While specific examples for the preparation of the products as found in dependent claims 24 and 29-36 are found in examples 3-10, these examples fail to provide any additional guidance or direction and merely list the amount of reactants, the compounds of the formula (II) and (III), for the preparation of the products of the formula (I), see, for example, page 81,

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example 4. There is no direction or guidance present on how to prepare the compounds of the formula (I) other than the general synthetic procedure starting on page 69. There is no direction or guidance present on the preparation of the formula (I) without the presence of an organic solvent and a coupling agent for the reaction of the compounds of the formula (II) and (III); no direction or guidance present for the preparation of the formula (II) without the presence of a solvent and a base for the reaction of the compounds of the formula (IV) and (V); nor is there any direction or guidance present for the preparation of the products of formula (II) with the presence of an organic solvent and a coupling agent with the reaction of the compounds of the formula (IV) and (V).

The breadth of the claims

The breadth of the claims is the preparation of the compounds of the formula (I) comprising reacting compounds of the formula (II) and (III) with or without the presence of an organic solvent and a coupling agent. The breadth of the claims also includes the preparation of the compounds of the formula (II) comprising reacting a compound of formula (IV) and formula (V) with or without the presence of a solvent or a base and (in dependent claims) with an organic solvent and a coupling agent for the preparation of the products of the formula (II).

The quantity of experimentation needed and the level of the skill in the art

While the level of the skill in the art is high, it would require undue experimentation to prepare the compounds of the formula (I) by reacting the compounds of the formula (II) and (III) without the inclusion of an organic solvent and a coupling agent as the instant specification only provides direction and guidance as to the

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preparation of the compounds of the formula (I) by the general synthetic procedure wherein the compounds of the formula (IV) and (V) are reacted in the presence of a base and a solvent to prepare the compound of the formula (II) which is then reacted with the compound of the formula (III) in the presence of an organic solvent and a coupling agent to prepare the compounds of the formula (I), see pages 69-71.

Furthermore, it would require undue experimentation to determine how to prepare the compound of the formula (II) by reacting the compounds of the formula (IV) and (V) without the use of a solvent and a base. It would also require undue experimentation as to the reaction of the compounds of the formulas (IV) and (V) with an organic solvent and a coupling agent as the specification does not provide any direction or guidance as to the reaction of the compounds of the formulas (IV) and (V) with an organic solvent and a coupling agent. It would require one of skill in the art undue experimentation to determine other possible reaction conditions, and required reagents and reactants to prepare the instant compound of the formula (I) without the presence of an organic solvent and a coupling agent for the reaction of the compounds of the formula (II) and (III) and without the presence of a solvent and a base for the reaction of the compounds of the formula (IV) and (V) for the preparation of the products of the formula (II).

Thus, the specification fails to provide sufficient support of the broad method of preparing the compound of the formula (I) comprising reacting a compound of the formula (II) and (III) and also fails to provide sufficient support of the broad method of preparing the compound of the formula (II) comprising reacting the compound of the formula (IV) and (V). There is also no support of the method of reacting the compounds

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of the formula (IV) and (V) in the presence of an organic solvent and a coupling agent for the preparation of products of the formula (II) as a result necessitating one of skill to perform an exhaustive search for which reactants/reagents and reaction conditions can be used to prepare the compounds of the formula (I) or (II) of the instant claims in order to practice the claimed invention.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001 , states that “ a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion” and “[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable”.

Therefore, in view of the Wands factors and In re Fisher (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to determine other methods of preparing the compound of the formula (I) by reacting the compounds of the formula (II) and (III) without an organic solvent and a coupling agent; to determine other methods of preparing the compound of the formula (II) by reacting the compounds of the formula (IV) and (V) without a solvent and a base; and to determine which organic solvents and coupling agents can be used to prepare the compound of the formula (II) by reacting the compounds of the formula (IV) and (V) in the presence of an organic solvent and a coupling agent, with no assurance of success.

This rejection can be overcome by including the presence of an organic solvent and a coupling agent in the process of claim 18, deleting claims 20-22, and including the presence of a solvent and a base in the process of claim 19.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 18-22, 24 and 29-36 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the presence of an organic solvent and a coupling agent for the reaction of the compounds of the formula (II) and (III) and the presence of a solvent and a base for the reaction of the compounds of the formula (IV) and (V). These omitted steps are critical or essential to the instantly claimed method as the specification only provides a description for the instantly claimed methods in the general synthetic procedure of pages 69-71 wherein the substituted 2-oxindole (formula IV) is reacted with the substituted 3-carboxy-5-formylpyrrole with a base and a solvent (page 69) and the 5-(2-oxo-1,2-dihydroindol-(3Z)-ylidenemethyl)-1-H-pyrrole-3-carboxylic acid (formula (II)) is reacted with formula (III) in an organic solvent and in the presence of a coupling agent (page 71). This rejection can be overcome by including the presence of an organic solvent and a coupling agent in the process of claim 18 and by including the presence of a solvent and a base in the process of claim 19.

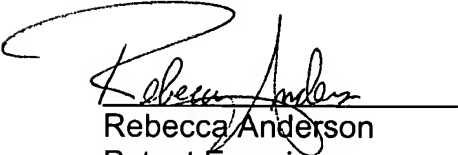
Conclusion

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Rebecca L. Anderson whose telephone number is (571) 272-0696. Mrs. Anderson can normally be reached Monday through Friday 5:30AM to 2:00PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Mr. Joseph K. McKane, can be reached at (571) 272-0699.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



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December 7, 2005